A New System of Automated Eco-genetic Database and Modern Conception of Prognosis of Bronchial Asthma

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ABSTRACT

The high epidemiological indexes of bronchial asthma (BA) and the high frequency of BA formation in early age groups, multiple genetic and external factors of phenotypic expression dictate the necessity of integrative study of eco-genetic characteristics of BA.

At present, it is widely recognized that hereditary predisposition is the main factor for the formation of BA. A unified assessment system of the cumulative impact of ecological and endogenous factors of BA does not exist on level of population or the individual.

The essential problem of modern medical prognosis is to work out an informational prognostic system.

We made formalized cards of BA primary and secondary prognosis based on the revealed complex of ecological, onto-genetical, clinical-laboratory and genotype and phenotype predictors.

The automatic prognostic system is formed by use of algorithm (consecutive statistic analysis of similar sings) according to the diminishing order of summary characteristic of predictors informational indices.

New and significant characteristic of the work is that based on the structure of ecological risk (nature of operation, genesis, intensity - attributive risk, duration of impact - cumulating risk) and genetic markers

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14. ABSTRACT

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(genealogical data, AB0, HLA and PI-genetic systems and other phenotypic markers) of BA, the formalized cards are recommended for the purpose of BA secondary prognosis differentiate for girls and boys.

The resulting automated assessment new system will allow carrying out processing personal data of genotypic and phenotypic characteristics and creating achievable, economical diagnostic and prevention methods of BA based on formalized cards.

The analysis of the data obtained has shown the relationship between the increasing prevalence rate of allergic diseases in children and the chemical air pollution intensity ($p<0,001$). In the districts with high air pollution intensity the earlier onset, heavier development of allergic diseases in children and the increase of the polyvalent sensitization frequency ($p<0,05$) have been recorded.

Thus, the obtained results indicate a significant influence of the air composition on the prevalence of allergic diseases and its growth with the pollution intensity in the dwelling district.

Problem Statement

Bronchial asthma problem has very high medical and social importance. At the same time still is very difficult to prevent this disease despite of good knowledge of Bronchial Asthma's(BA) pathogenesis and triggers of attacks. Sometimes doctors are unable to manage well this pathology, because of neglected early diagnostic. According to the most actual and perspective direction of nowadays allergology it is working out new scientific approach of resolution of bronchial asthma problems in young population.

The high epidemiological indexes of BA and high frequency of BA formation in young age groups are occurred in the last period in Georgia as well in the whole world. Influence of multiple factors on prevalence of disease: influence of external and internal risk-factors, genetic predisposition to developing BA dictate the necessity of integrative study of ecological-genetic study of BA.

At present it is widely recognized that hereditary predisposition plays the most important role in the developing of disease. But hereditary predisposition is not everything recognizable by physicians because it is not demonstrated by clinically manifested asthma in parents and other close relatives of affected individual.

Hence to above mentioned, reveal of young individuals having maximum risk of BA is the milestone of preventive measurements and early diagnostic of BA. It means that we talk about prognostic of BA among young individuals who have not any symptoms of disease before and according their medical history they are practically healthy. Primary prognostic of disease like BA is early diagnostic in fact. This is priority approach of Public health.

Georgian Armed Forces is been forming now. One of the most important problem of nowadays military medicine very high morbidity of military personnel. Despite the fact that the scale and quality of conscripts' medical investigation, that is being done at the moment of recruiting, is far from required standards, - above mentioned morbidity level is a little bit unexpected.

We have done randomized investigation of patients' histories in Central Military Hospital (Tbilisi) and Military Outpatient Clinic (Tbilisi) for the last 5 years period: 1998-2003. Among the frequently revealed diseases, are allergic disorders: urticaria, Quinke's oedema, chronicle rhinitis, conjunctivitis and bronchial asthma. Above mentioned diseases often became the causes of soldiers' retention from the army. Their frequency are as well high in the civil population of similar age group.

In conditions of a substantial increase in bronchial asthma incidence rate epidemiological and investigations become very important. It should be mentioned that none of the official documents of WHO and European international societies gives information on epidemiological investigations carried out in the former USSR. This can be explained, in official data such as low level of the bronchial asthma incidence rate is given that this figures are regarded as rather doubtful. In order to obtain impartial information on bronchial asthma in adolescent and young population in Tbilisi a prospective epidemiological investigation has been carried out.

Materials and methods

It was investigated 184 families, among them: 171 young persons, aged 12-20 years with Bronchial Asthma, 26 sybses and 295 parents. 134 young patients were investigated with deep medical (specific allergologic) investigation:

1. Allergologic anamnesis was studying by special scheme elaborated in Russian Scientific Research Institute of Allergology
2. Allergic skin tests: was performed according above-mentioned Institutes' recommendations
3. Study of individuals' immunologic status: determination of T-Lymphocytes subpopulations by monoclonal antibodies by using laser fluoro-cytometric method, determination of IgA, IgM, IgG, was performed by using method of radial immunes-diffusion, and total IgE – by using radio-immunological method
4. Program providing : CH program language, using R:BASE interface
5. Clinical-genealogic method (Falconer D., 1965): study of genealogical tree of investigated families.
6. Choosing of markers: it was used to approaches: 1. seeking of phenotype markers, that is characterized with high significance of mathematical magnitude and 2. seeking of genotype markers that is genetically associated with disease.

I. Investigation of genotypic and phenotypic markers:

1. Erythrocyte markers: ABO, Rhesus systems was determined by standard serums,
2. Leukocyte markers: HLA system's markers were determined Terosoki's (micro –lymphocyte-toxic tests) typing was performed with 1st class (A, B, C) antigens and 2nd class (DR, DQ) locus's
3. Phenotyping of PI genes was performed using iso-electric focusing in poly-acrilamid gel
4. Anthropometric investigations:
   - **a.** Height/weight ratio at birth
   - **b.** Eye's and hair's colour: it was determined three basic types of eye colour: bright: blue, grey; Transitional: green, greenish-brown; Dark: black, dark brown. and three basic hair colors: bright: blond, light chestnut, dark chestnut, black;
5. Phenotype signs:
   - **a. Morphologic signs**:
     - i. Pinna's lower lobe type,
     - ii. Type and location of vortex on the head: it exists six types of this sign: 1. centred and clockwise directed, 2. centred and counter clockwise directed, 3. located at right and clockwise directed, 4. located at right and counter clockwise directed, 5. located at left and clockwise directed, 6. located at left and counter clockwise directed.
     - iii. Dermatogliphical data: picture of palm lines.
   - **b. Physiological signs:**
     - i. Ability to turn a tong into tube
     - ii. Type of finger's crossing: left and right type
     - iii. Hand's crossing type: left and right type
   - **c. Ear-wax type:** it was determining by otoscopic method:
     - i. Dry ear-wax type

ii. Wet ear-wax type

d. Stigmas: minor congenital, multi-factorial defects. They rarely are caused by teratogenic action of drugs.

II. Method of genetical ans statistical analyze;

III. Method of multi-dimensional phenotyping: algometric- hierarchic(al) cluster analyze of chosen systems of signs. Analyze was performed in the interactive order.

By this method we have determined four types of phenotype classes:

1. Classes of basic predisposition, including up to 80% of individuals with manifested asthma;
2. Classes of relative predisposition, including less then 80% of individuals with manifested asthma;
3. Phenotype classes including a few patients
4. Phenotype classes not predisposed to BA, basically including healthy persons.

Results and discussion:

Questioning and medical examination have shown that in the investigated contingent 184 persons have clinically manifested BA with different severity. Among them - 119 (65,4%) were males and 55 (35,6%) - females. 32,7% of patients had severe BA, 62,6% - moderate BA and 4,7% - mild BA. Investigation of this groups revealed that all significant risk factors of BA were present: atopic diathesis, nutritional allergy, drug-induced allergy, asphyxia of foetus or newborn child, pathological pregnancy and pathological delivery.

Fig 1.

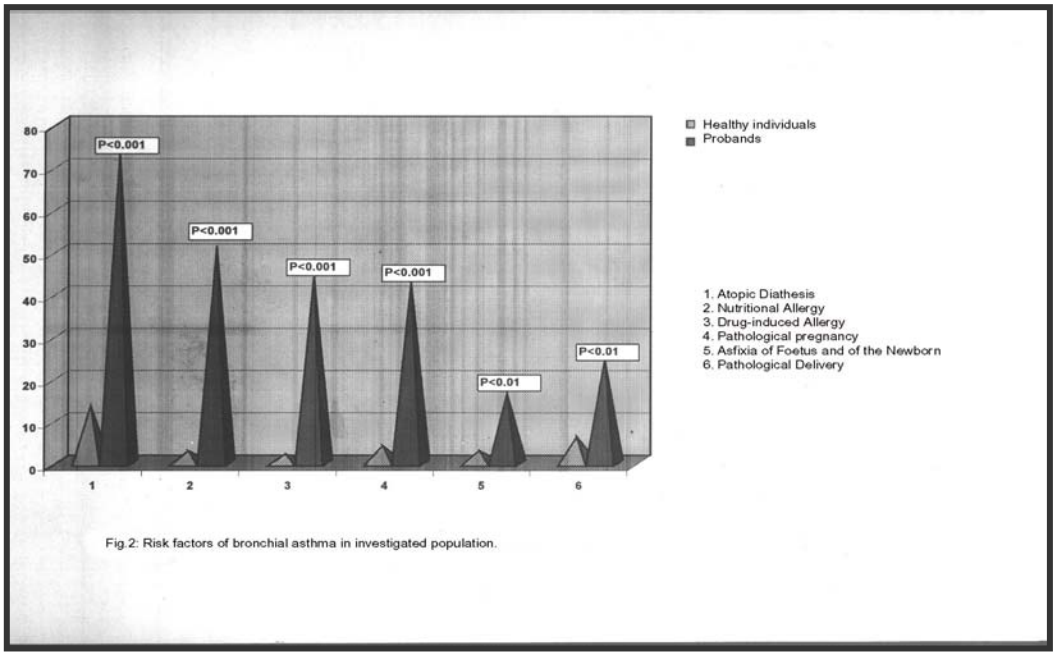

Fig.2: Risk factors of bronchial asthma in investigated population.

Phenotypic characteristics of investigated contingent showed that young persons with BA have the following phenotypical peculiarities: 1) High height-weight indexes at the birth moment: M^+ (13,7% in the basic and 7% in the control group, P<0.001), and M°/ M^+ (39,5% and 17,1%, P<0.01); 2) Fair hairs (29,4% and 20,7%, P,0,01): 3) Bright eyes (24.4% and 15,5%, P<0.001); 4) Absence of ability of turning

tongue into tube (66,3%, P<0,001), 5) Type of vortex on the head: centered and anticlockwise directed (44,1%, P<0,001) and located at right and anticlockwise directed, 6) Dermatoglifiks: significant rising of frequency of ulnar stitch encountering (63,5%, P<0,005), absence of "C" three-radius (11,0%, P<0.01) compare with control group. Besides dry earwax gene encountering in investigated group have significantly increased, whereas wet earwax gene encountering was twice more less in healthy persons. There was revealed significant positive BA predictors, that are associated with disease, particularly 0 (I) of ABO group (RR=1,75,P<0.01) It was revealed high authentic positive association of BA with antigen B7 (RR=15,12; P<0,001) and DR5 (RR=8,42, p<0,0001) .

Fig. 2

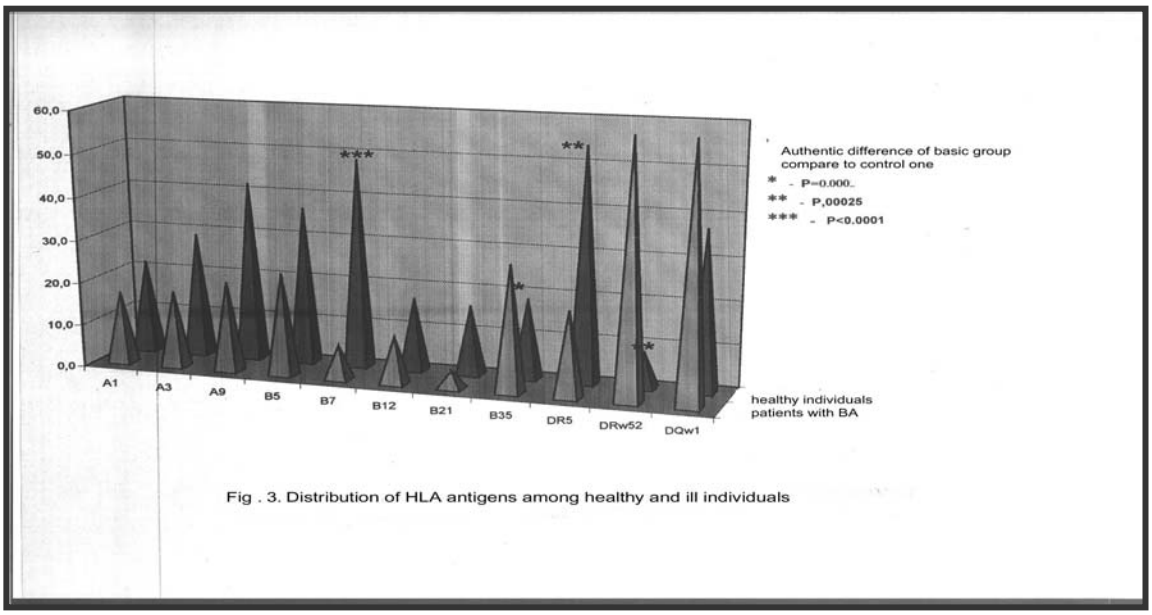

Fig . 3. Distribution of HLA antigens among healthy and ill individuals

Fig.3

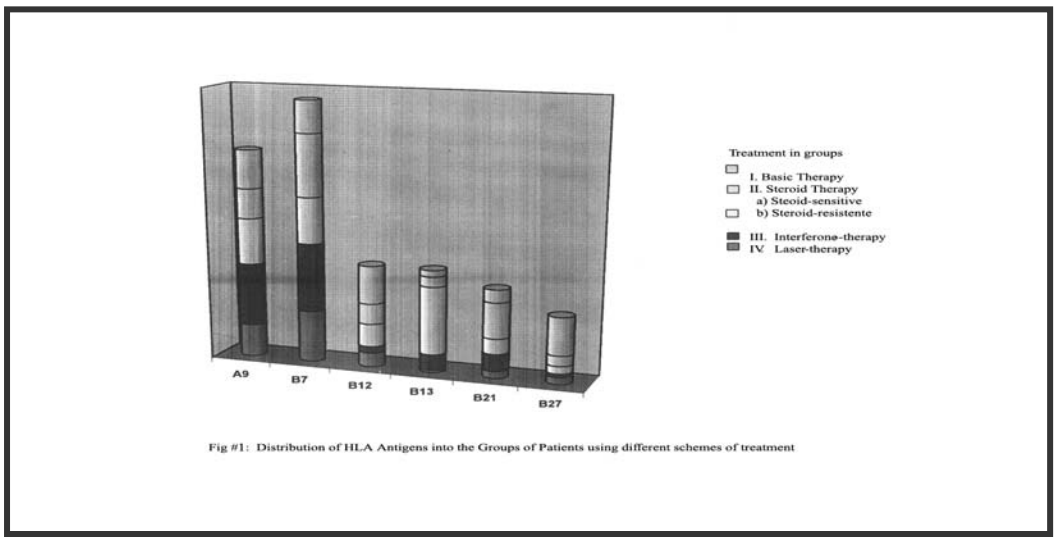

Fig #1: Distribution of HLA Antigens into the Groups of Patients using different schemes of treatment

In the table #1 is shown the tabulation of the significant phenotypic signs.

table #1 **Volume and Quality of Performed Investigation in the Targeted Contingent**

#	Performed investigation	Investigated Contingent			Total number of investigated persons
		Probands	Parents and Sybces	Control group	
1	**Clinical and Genealogic Investigation**	184	321	793	505
2	**Anthropometry:**	212	1002	793	2007
	a. height and weight indexes at the birth moment	212	1002	793	2007
	b. color of yes and hairs	184	321	116	621
	c. location of the vortex on the head	184	321	116	621
	Phenotypical Indexes				
3	**Morphological:**				
	a. Pinna's lower lobe type	184	321	116	621
	b. dermatoglifics	184	321	116	621
4	**Physiological:**				
	a. ability to tube a tongue	184	321	116	621
	b. type of hand crossing	184	321	116	621
5	**Stigmas**	184	321	116	621
	Genes markers				
6	**Type of earwax (cerumen)**	184	321	116	621
7	**Erythrocytes Antigen System:**				
	a. ABO system	220	1002	793	2015
	b. Rhesus system	220	1002	793	2015
	c. MNS system	96	321	214	631
	d. P system	98	321	214	
8	**Leukocyte Antigen System:**				
	HLA system	117	-	200	317
9	**PI – Phenotyping**	117	15	200	332

For establishment of phenotypic structure of population using multi-dimensional phenotyping it was determining for each predictor: statistical index between healthy and ill individuals (t-criteria by Student). genetic association of signs with BA, heredity factor (h^2) and integrity of markers.

Wile resuming investigation results, it have to be mentioned that the worked out computing table is enough simple and opportune (handly) for comprehensive use. It is proposed, for primary prognostic of BA, to practical doctors working in outpatient clinics and dispensaries, as well for military doctors working with enlistment committee or in military units. This method gives the possibility for prognosis predisposition to bronchial asthma in young population.

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SYMPOSIA DISCUSSION - PAPER 14

Authors Name: Prof. Karseladze (Dr Goderdzishvili speaker) (Georgia)

Discussor's Name: Unknown

Question:
Did you investigate use of cigarette smoking in participants and family members?

Author's Reply:
We did not investigate use of cigarette smoking, because the aim of work was to evaluate the role of genetic and phenotype markers and their combinations in early diagnosis and prognosis of BA (Bronchial Asthma). But we plan to continue to study the problem of COPD in military personnel. In the initial questionnaire there are questions included concerning cigarette smoking. Cigarette smoking is an external risk-factor and trigger of COPD.

Authors Name: Prof. Karseladze (Dr Goderdzishvili speaker) (Georgia)

Discussor's Name: Dr Barrett (UK)

Question:
Are any steps being taken either by Government or Industry to reduce level of pollution in highly polluted areas?

Author's Reply:
No – but with our new Government comes a promise to be more attentive and we are going to present our results to national authorities. We hope our recommendations will influence on their decisions to improve the ecological situation in Tbilisi.